

REMARKS

Claims 1-19 are pending in this application and were subject to a restriction requirement. Claims 12-16 are withdrawn from consideration by election filed on July 21, 2004. Claims 1-11 and 17-19 stand rejected. Claims 5, 8, and 19 are objected to. Claims 1, 3-6, 8, and 19 are amended herein. Support for amended claims can be found, for example, at page 3, lines 1-18 and page 8, line 29 through page 9 lines 15 of the specification as well as throughout the examples and claims as originally filed. Claims 2 and 9 are cancelled herein without prejudice or disclaimer. Thus, no new matter is added.

Claim Objections

Claims 5 and 8 are objected to because there are no spaces separating the terms "1H,3H,11B,13C,15N,19F,29S." The Applicants amends these claims to add a space between each of these terms. Claim 19 is objected to for reciting "one or mixture of chemical compounds." The Applicant amends claim 19 herein to recite "one or a mixture of chemical compounds," as the Examiner suggests. The Applicant respectfully submits that by correcting these informalities these claims are in condition for allowance, and removal of these objections is respectfully requested.

35 U.S.C. § 112, first paragraph

Claims 1-11 and 17-19 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with written description. In particular, the Examiner alleges that the Applicant has not provided written description for methods of detecting compounds that interact with a target molecule wherein the target molecule is not an enzyme. Furthermore, the Examiner alleges that the present invention relates only to methods using one-dimensional and multi-dimensional NMR rather than any spectroscopic technique. The Applicant respectfully submits that the specification provides adequate written description for methods using target molecules other than enzymes or spectroscopic techniques other than NMR for identifying chemical compounds that interact with a target molecule. However, in an effort to advance prosecution and in no way acquiescing to the Examiner's allegation, the Applicant amends claims 1 and 19 herein to recite "enzyme" rather than "target molecule" and to specify "NMR" spectra or spectrum. Accordingly, claims 2 and 9 are cancelled herein, thus, rendering rejection of these claims moot.

The Applicant respectfully submits that in view of the forgoing remarks and the claims as amended, the Applicant has overcome the Examiner's rejection under 35 U.S.C. § 112, first paragraph for independent claims 1 and 19 and that these rejections should be withdrawn. Claims 2 and 9 are cancelled herein, thus, rendering rejection of these claims moot. As claims 3-8, 10, 17 and 18 depend from claim 1,

either directly or indirectly, Applicant believes rejection of these claims has been overcome and that they should also be withdrawn.

35 U.S.C. § 112, second paragraph

Claims 1-11 and 17-19 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite for failing to point out the subject matter the Applicant regards as the invention. Specifically, the Examiner alleges that the language “at least one chemical compounds” in claim 1 renders the claim vague. The Examiner also alleges that the recitation “a target, a target molecule, the target molecule and “said target molecule” in claim 1 is uncertain. The recitation “the transformation” in claim 1 allegedly lacks antecedent bases. Furthermore the Examiner alleges that the recitations “a target” in claim 2 and “a chemical compound” in claim 3 lack antecedent bases. The Examiner also alleges that the terms “a first spectrum” of claim 4, “a mixture” of claim 6, and a “target molecule” of claim 19 lack antecedent basis. Finally, the Examiner points out that claims 5 and 8 recite Markush groups with improper language and that claim 19 recites language that is “confusing.” The Applicant amends claims 1, 3-6, 8, and 19 herein to clarify the language of each amended claim. Specifically, the Applicants amends claim 1 and 19 to recite the term “enzyme” instead of “target molecule.” Claims 2 and 9 are cancelled herein, thus rendering rejection of these claims moot.

The Applicant respectfully submits that in view of the forgoing remarks and the claims as amended, the Applicant has overcome the Examiner's rejection under 35 U.S.C. § 112, second paragraph. The Applicant respectfully requests that rejection of claims 1, 3-8, 10-11, and 17-19 be withdrawn.

35 U.S.C. § 102

Claims 1-4, 6, 7, 9-11, 17, 18, and 19 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Moore, *et al.* U.S. 2003/0143757 (hereinafter “Moore, *et al.*”). The Examiner maintains his rejection of July 28, 2005, finding the Applicant's arguments of October 18, 2005 unpersuasive. Specifically, the Examiner alleges that Moore, *et al.* teach “generating a spectrum of nicotinic acid and 2-phenoxy benzoic acid after exposure to the target molecule of p38 MAP kinase.” A single prior art reference anticipates a claimed invention only if it identically shows every element of the claimed invention. *In re Bond*, 15 U.S.P.Q.2d 1566 (Fed. Cir. 1990). The Applicant respectfully submits that Moore, *et al.* merely disclose a mixture of chemical compounds with or without a target molecule, where the compounds may be ligands of the target molecule. See, for instance, page 2, column 1 paragraph 0016 of Moore, *et al.* The Applicant amends claims 1 and 19 herein to recite “an enzyme” rather than a “target molecule.” The Applicant also removed the term “ligand” from these claims in a previous amendment. As is understood in the art and as is disclosed in the specification, at for example page 9, lines 1-10 of the present specification, substrates

are molecules that may be catalytically converted by enzymes to products. Thus, claims 1 and 19, as amended, relate specifically to methods of identifying chemical compounds that interact with an enzyme comprising measuring at least one NMR spectra of a substrate or product of the enzyme. Moore, *et al.* do not contemplate exposing substrate or product to an enzyme with chemical compounds and generating a spectrum of the substrate or product. Moore, *et al.* merely disclose obtaining spectra of drug cores with a target molecule. Thus, Moore, *et al.* do not identically show each and every element of the independent claims of this invention.

In addition, claims 1-11, 18 and 19 stand rejected under 35 U.S.C. 102(b) as being anticipated by Thompson *et al.*, *Proc. Natl. Acad. USA*, Vol. 94 pp. 14249-14254 (Dec. 1997) for reasons of record. Specifically, the Examiner alleges that the Applicant does not indicate whether or how the terms “substrate” or “product” distinguish over the art. The Applicant respectfully submits that the specification discloses at page 8, line 29 through page 9, line 15 a detailed description of enzyme, substrate and product kinetics. Furthermore, as pointed out above, the skilled artisan understands the relationship of a given enzyme with respect to its substrate and product. Thompson, *et al.* disclose only a double-labeled inhibitor alone or with cathepsin K followed by a ¹⁵N-decoupled spectrum of the same mixture (see figure 4 a-c in Thompson, *et al.*). These spectra are of the inhibitor (i.e., chemical compound) not of substrate or product. Thus, the Applicant respectfully submits that because Thompson, *et al.* do not disclose methods of identifying chemical compound that interact with an enzyme comprising detecting substrate and/or product, they do not disclose each and every element of the claims.

Claims 1-11, 18 and 19 stand rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Hajduk, *et al.* *J. Am. Chem. Soc.* 1997 Vol. 119 pp. 12257-12261. Specifically, the Examiner maintains his allegation that Hajduk, *et al.* teach “identifying compounds that bind to macromolecules by one-dimensional NMR.” As noted above, claims 1 and 19 are amended herein to recite “enzyme” rather than “target molecule.” Also, as noted above, substrate and product are discussed in the specification as well as understood in the art. The Applicant respectfully submits that Hajduk, *et al.* rely on chemical compound spectra only in the presence and absence of FKBP. They do not disclose spectra of a substrate or product of an enzyme. Thus, Hajduk, *et al.* do not teach each and every element of the instantly claimed invention.

Claims 1-4, 6, 7, 9-11, 17 and 19 also stand rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Fesik, *et al.* (WO 98/48264 hereinafter “Fesik, *et al.* I”). Specifically, the Examiner maintains his allegation that Fesik, *et al.* I teach generating a diffusion-filtered proton spectrum of “one or a mixture of chemical compounds,” exposing one or a mixture of compounds to a target and comparing the first and second spectra. As discussed throughout this response, the Applicant amends claims 1 and 19 to recite “enzyme.” Furthermore, the Applicant submits that the terms “substrate” and “product” with respect to a given enzyme are described in the specification and understood in the art. The Applicant respectfully

submits that Fesik, *et al.* I merely disclose a comparison of a spectrum of chemical compound alone with a spectrum of chemical compound mixed with target molecule, wherein the presence of target molecule significantly effects T2 relaxation time of residual peaks on the compound. Thus, Fesik *et al.* I only disclose obtaining spectra of chemical compounds but not of substrate or product of an enzyme. More importantly, they do not disclose obtaining at least one spectrum of the substrate or product to identify compounds that interact with an enzyme in a mixture comprising enzyme, chemical compound and substrate or product of the enzyme. Thus, Fesik, *et al.* I do not teach each and every element of the instantly claimed invention.

Claims 1-4, 6, 7, 9-11, 17 and 19 also stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Fesik, *et al.* (WO 97/18469 hereinafter “Fesik, *et al.* II”). The Examiner again maintains his allegations that Fesik, *et al.* II teach screening chemical compounds for binding a given target molecule using a ¹⁵N/¹H NMR correlation spectrum. The Examiner also finds the Applicant’s arguments, filed on October 18, 2005, in relation to this reference, unpersuasive. Furthermore, the Examiner alleges that the Applicant does not indicate “wherein or how the terms ‘substrate’ or ‘product’ distinguish over the art.” With respect to the meaning of these terms, the Applicant discusses these terms as they are known in the art and in described in the specification herein. More importantly, Fesik, *et al.* II disclose spectra of the **target molecule** (i.e., a large biomolecule) only and not of a **substrate or product**. The spectrum disclosed in Fesik II is two-dimensional spectrum of the target molecule or protein in the presence or absence of an interactive chemical compound. There is no disclosure of obtaining a spectrum of the substrate or product of an enzyme. Thus, Fesik, *et al.* II do not teach each and every element of the instantly claimed invention.

Finally, claims 1, 2, 4-10, 18 and 19 stand rejected under 102(a) as being anticipated by Bleicher, *et al.*, *J Org, Chem* (1998) 63:8486-8490. Specifically, the Examiner alleges that Bleicher, *et al.* teach:

a target molecule that is vancomycin; one and two dimensional first and second spectrum; shifting of ¹H; a mixture of 2 and 100 chemical compounds; 256 scans, which read on incubation times greater than 50; NMR spectra; a determining step by visual inspection; and apparent quenching of the reaction at a selected time.

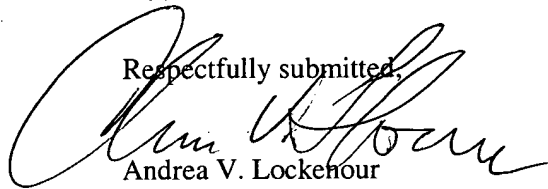
The Applicant respectfully submits that in Bleicher, *et al.* do not disclose enzyme, substrate or product. They merely disclose using DECODES spectroscopy to detect interactions of vancomycin with peptides using TOCSY NMR analysis. The Applicants further submit that the peptides described by Bleicher, *et al.* are short sequences that do not act as enzymes or functional proteins, but merely serve as “ligands” for the larger vancomycin. Finally, the Applicant points out that Bleicher, *et al.* describe vancomycin as a target molecule and the peptides with which it interacts as “ligands,” but they do not disclose measuring the interaction of an enzyme with a chemical compound by measuring the substrate or

product of the enzyme using NMR spectroscopy. Thus, Bleicher, *et al.* do not teach each and every element of the instantly claimed invention.

The Applicant respectfully submits that in view of the forgoing remarks and the claims as amended, the Applicant has overcome the Examiner's rejection under 35 U.S.C. §102. Claims 2 and 9 are cancelled herein, thus, rendering rejection of these claims moot. The Applicant respectfully requests that rejection of claims 1, 3-8, 10-11, and 17-19 be withdrawn.

The Applicant reserves the right to prosecute, in one or more patent applications, the claims to non-elected inventions, the cancelled claims, the claims as originally filed, and any other claims supported by the specification. The Applicant thanks the Examiner for the Office Action and believes this response to be a full and complete response to such Office Action. Accordingly, favorable reconsideration and allowance of the pending claims is earnestly solicited. If it would expedite the prosecution of this application, the Examiner is invited to confer with the Applicant's undersigned attorney.

Respectfully submitted,



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